REMARKS

An election under 35 U.S.C. § 121 has been required to the subject matter of:

Group (I) Claims 1 to 14, 21, 35, 23, and 30 drawn to a vector comprising a LMW PEI and a DNA, and methods of making the vector, classified in class 435, subclass 320.1;

Group (II) Claims 30, 38 and 39, drawn to pharmaceutical compositions comprising a LMW PEI and a DNA, and an *in vivo* gene therapy method comprising the step of administering to any subject a vector comprising a LMW PEI and a DNA, classified in class 514, subclass 44;

Group (III) Claims 24, 25, 33, 36 and 40 to 43, drawn to transfected cell comprising the vector, and *in vitro* methods for making the transfected cells, and *ex vivo* gene therapy method comprising the step of administering to any subject genetically modified cells expressing a DNA which is transfected by a vector comprising a LMW PEI and the DNA, classified in class 435, subclass 325, and class 424, subclass 93.21; and

Group (IV) Claims 15 to 19, 32, 34 and 37, drawn to a process for preparing a LMW PEI, pharmaceutical compositions comprising the LMW PEI, classified in class 424, 486.

In response to the restriction requirement, Applicants provisionally elect **Group I** for further prosecution in this application encompassing claims 1 to 14, 21, 35, 23, and 30 drawn to a vector comprising a LMW PEI and a DNA, and methods of making the vector.

This election is made *with traverse* and is made without prejudice to Applicants' right to file divisional applications directed to the non-elected subject matter. It is respectfully requested that the restriction requirement be favorably reconsidered and withdrawn.

The Office Action further requires a "three-tiered" election of species (if Applicants elect the claims of Group I) with respect to the following patentably distinct species:

Species Election I:

(a) the vector of claim 1, which is a viral nucleic construct and
(b) the vector of claim 1, which is a non viral construct;

Species Election II:

(a) the effector gene of claims 7, 8, and 9, in which the effector gene is selected from the group consisting of the coding sequence of a pharmacological active compound or its prodrug form,
(b) the coding sequence of an enzyme, and
(c) the coding sequence of a fusion protein comprising an enzyme fused to a cell-specific ligand; and

Species Election III:

(a) the vector of claim 1, wherein the ratio by weight of LMW PEI to nucleic acid is 3: 1 or more; and
(b) the vector of claim 1, wherein the ratio by weight of LMW PEI to nucleic acid is 8:1 or more.

In response to this three-tiered species election requirement, Applicants elect the following species for further searching in this application:

I (a) the vector of claim 1 which is a non viral construct;

II (c) the vector of claim 9, wherein at least one effector gene is expressed together with a cell-specific ligand as a fusion protein; and

III (a) the vector of claim 1, wherein the ratio of weight of LMW PEI to nucleic acids is 3:1 or more.

Claims 1 to 14 are readable upon the elected species.

The requirement for this three-tiered election of species is also respectfully traversed since the species are each related to one another and directed to the same inventive concept which may be searched simultaneously. It is Applicants' understanding that upon the allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all of the limitations of an allowed generic claim as provided by 37 C.F.R. 1.141.

It is respectfully noted that it would not be an undue burden on the Patent Office to search all the pending claims in a single application. Accordingly, it is submitted that the restriction requirement and species election are improper and should be reconsidered and withdrawn.

The MPEP lists two criteria for a proper restriction requirement. First, the inventions must be independent or distinct. MPEP § 803. Second, searching the additional inventions must constitute an undue burden on the examiner if restriction is not required. *Id.* The MPEP directs the search and examination of an entire application "[i]f the search and examination of an entire application can be made without serious burden, ...even though it includes claims to distinct or independent inventions." *Id.*

The Office Action states that the subject matter of Groups I, II, III and IV are distinct inventions which have acquired separate status in the art due to their recognized divergent subject matter. In particular, it is alleged that the *ex vivo* gene therapy claimed in Group III employs materially distinct steps, e.g., administration of genetically modified cells expressing a therapeutic protein and/or DNA, and the *in vivo* gene therapy cited in Group II comprises materially distinct steps, e.g., *in vivo* administration of DNA sequences encoding a therapeutic protein and/or DNA to a subject or target cells from the subject and thus, the materially distinct steps generate different modes of operation and different effects. Further, the Office Action claims that the vectors of Group I are not limited in the processes cited in Groups II and III and can be used for production of protein molecules and/or antibodies *in vitro*. Further, the Office Action states that the combination of Group I which are also encompassed by the claimed processes of Groups III and IV does not require the particulars of the subcombination as claimed in Group IV and that the specific subcombination as recited in the Group IV has separate utility in the delivery of drugs and proteins.

The present invention is directed to a polyethylenimine ("PEI") which has a molecular weight of less than 50,000 Daltons (low molecular weight PEI – "LMW PEI") and a vector which contains the LMW PEI and a nucleotide sequence, to the methods and processes for preparing the LMW PEI and to uses of LMW PEI in a complex with a viral and non-viral

nucleotide sequence for insertion into a cell. This invention also relates to the administration of these transfected cells to a mammal for achieving the prophylaxis or therapy of a disease and to the administration of LMW PEI in a complex with a nucleic acid sequence to a mammal for achieving the prophylaxis or therapy of a disease. The nucleic acid of the present invention can be an oligonucleotide or a nucleic acid construct, which can contain one or more effector genes encoding for a pharmaceutically active compound and/or an enzyme. The vector of the present invention can further contain a cell-specific or target-specific ligand. The invention is further directed to the process for preparing a transfected cell and the use of the transfected cells as a pharmaceutical and/or in gene therapy.

Applicants respectfully submit that the claims of Groups I to IV should not be subject to restriction as they are all related and are directed to the same inventive concept. The vectors of Group I are constructed with the LMW PEI produced by the processes of Group IV. Further, the pharmaceutical compositions and gene therapy methods of Group II and the transfected cells, methods for their production and the gene therapy methods associated with the transfected cells of Group III are all related to the vectors containing LMW PEI and the claims of Groups I and IV. Therefore, all of the compositions, processes and methods are related to the same inventive concept.

It is also respectfully submitted that the claims in Groups I to IV may be searched and examined together without serious burden as they all relate to the vectors comprising LMW PEI and a DNA claimed in Group I. For example, the pharmaceutical compositions and the *in vivo* gene therapy methods claimed in Group II are relate to the vectors of Group I. In particular, the *in vivo* gene therapy methods comprise the step of administering the vectors of Group I. Searching the claims of Group I would necessarily overlap and include a search of the individual pharmaceutical compositions and gene therapy methods using the vectors in Groups II and III.

Similarly, searching the LMW PEI as contained in the vectors of Group I, would necessarily overlap and include a search of the processes for preparing LMW PEI and the pharmaceutical compositions comprising LMW PEI of Group IV.

In view of the similarity among claims 1 to 19, 21, 23 to 25 and 30 to 43, it is submitted that a search of the prior art when examining the claims of Group I would, at the same time, result in a search of prior art for use in examining all the remaining claims of the application.

The claims in Groups I, II and III are related as product and processes of use. The MPEP provides that inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different products, or (2) that the product as claimed can be made by another and materially different process (MPEP 806.05(f)).

Applicants respectfully assert that the inventions of Groups I to III are related and that the requirements of the two-part test are not fulfilled. According to part (1) of the test, the inventions are distinct if the process can be used to make other and materially different products. The fact that the vectors of Group I can be used for the *in vitro* production of proteins and/or antibodies does not render the processes of Groups II and III separate and distinct from the vectors of Group I. In evaluating other possible methods, it should be considered that not all proteins and/or antibodies that can be produced *in vitro* can be produced by *in vivo* methods. The pharmaceutical compositions and *in vivo* gene therapy methods of Group II and the transfected cells, the *in vitro* methods for making those cells, and the *ex vivo* gene therapy method of Group III specifically required the vectors of Group I to practice the claims of Groups II and III, and per se, the processes cannot be used to make other and materially different products.

For the foregoing reasons, the restriction requirement should be withdrawn at least with respect to the Groups II and III, as they relate to the vectors claimed in Group I.

Groups I, II, III, and IV are related as combination and subcombination. The MPEP also provides that inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP 806.05(c)). The Office Action alleges that the combination of Group I which are also encompassed by the claimed processes of Groups III and IV does not require the particulars of the subcombination as claimed in Group IV, e.g., addition of boron triflouride rather than addition of acid catalysts and that the specific subcombination as recited in the Group IV has separate utility such as the use of the LMW PEI prepared by the process of claim 19 in the delivery of drugs and proteins.

With respect to Group IV, the claims are directed to processes for preparing a LMW PEI and pharmaceutical compositions comprising the LMW PEI. The LMW PEI is combined with DNA to form the vectors claimed in Group I. Applicants assert that the methods of preparing and using the LMW PEI are novel and nonobvious, the vectors that incorporate LMW PEI are also novel and that the methods of using LMW PEI compositions and vectors incorporating the LMW PEI should be examined together in one application.

One of skill in the art would appreciate that the vectors as claimed in Group I, including LMW PEI as produced by the processes of Group IV and a DNA, would be utilized to produce the compositions and transfected cells in Groups II and III, and that the vectors produced by the methods of Group I may be used to practice the various methods of Groups II and III. Thus, it is respectfully asserted that the claims of Groups I, II, III and IV should be

joined together, since the Group I search would encompass a search and examination of the claims in Groups II through IV.

If the restriction requirement is maintained, it is submitted that duplicate searching of the various Groups in separate divisional applications would be quite inefficient to the operation of the Patent and Trademark Office. It would therefore be most beneficial for both efficiency and cost savings to the Applicant, as well as the PTO, for this case to proceed without restriction.

Furthermore, it is likely that the same Examiner would be in charge of the divisional cases, but since these divisional applications would be examined at a much later date, the Examiner will have to conduct a duplicate, redundant search at the time he examines the divisional cases. Alternatively, if a different Examiner is assigned to the divisional applications, a significant loss of PTO efficiency would be incurred as a results of the examination of divisional cases.

It is respectfully urged that restricting the claims in the manner suggested in the restriction requirement constitutes an undue burden to Applicants. If followed, the restriction requirement would require Applicants to file a number of additional applications. The cost of prosecuting and maintaining additional patents is unreasonable in view of the fact that the application as filed includes claims that are all related to one another. Further, under GATT, the period of exclusivity for any patents which issue from these divisional applications is greatly reduced. In addition, the public is inconvenienced as they will not know whether or not Applicants will file divisional applications to the remaining subject matter. Accordingly, the public will not know if they can practice the remaining invention without infringing future patent applications.

In order to be fully responsive to the Office Action, Applicants have responded to the "three-tiered" species election, but Applicants are unclear as to why this species election is necessary. The vectors of claims 1 to 14 are all drawn to vectors comprising a LMW PEI and a DNA. Applicants do not understand how the selection of a specific vector characterized by the three species elections will facilitate searching this Application, as any of the combinations selected from the three-tiered species election would result in the same search being conducted. Applicants have made the election from the three specific vector characteristics required by the Examiner in order to advance prosecution of this Application, but expressly reserve the right to file divisional applications direct to the non-elected subject matter.

In view of the foregoing, Applicants respectfully request that the restriction requirement and species election as to claims 1 to 19, 21, 23 to 25 and 30 to 43 be reconsidered and withdrawn and respectfully submit that all of the claims should properly be examined in one application. Early and favorable examination of claims 1 to 19, 21, 23 to 25 and 30 to 43 in this application is respectfully requested.

This paper is being timely filed and no fee is believed to be due. However, if any fee is determined to be due, the Assistant Commissioner is authorized to charge such fee, or credit any overpayment, to Deposit Account No. 50-0320.

Respectfully submitted,
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